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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,576	10/17/2005	Mitsuharu Hirai	TOYA114.008APC	4658
20995 7590 10/25/2007 KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			EXAMINER STAPLES, MARK	
			ART UNIT 1637	PAPER NUMBER
			NOTIFICATION DATE 10/25/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/553,576	Applicant(s) HIRAI, MITSU HARU	
	Examiner Mark Staples	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
 4a) Of the above claim(s) 1-17 and 22-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-21 is/are rejected.
- 7) ☒ Claim(s) 18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11/09/05, 12/15/06, & 03/23/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of claims 18-21 in part of Group XII and SEQ ID NO: 22 in the reply filed on 09/24/2007 is acknowledged. The traversal is on the ground(s) that SEQ ID NO: 21 would not create an additional search burden. This is found persuasive.

Claims 1-17 and 22-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 09/24/2007.

In summary, claim 18-21 in part with elections of subgroups SEQ ID NOs. 21 and 22 will be fully examined for patentability.

Specification

2. The abstract of the disclosure is objected to because there is no complete sentence and the abstract should not replicate a claim(s). Correction is required. See MPEP § 608.01(b).

Sequence Rules Compliance

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To

Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given time of reply to this office action within which to comply with the sequence rules, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in **abandonment** of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Figures 4 and 5 respectively contain sequences without SEQ ID NOs. If these sequences are included in the sequence listing provide by Applicant, the specification should be amended to include the SEQ ID NOs. If these sequences were not included in the sequence listing filed 10/28/2005, Applicant should provide a substitute sequence listing and a CRF that include those sequences.

Claim Objections

4. Claim 18 is objected to because of the following informalities: the claim refers to non-elected claim 16. Claim 18 should directly recite SEQ ID NO: 21 and SEQ ID NO: 22. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Critchley (WO 02/072875 published 19.09.2002) and Buck et al. (1999); as evidenced by Froguel et al. (1993) and by Howell et al. (1999).

Regarding claim 18, Critchley teaches methods for detecting a mutation comprising:
performing a melting curve analysis for a nucleic acid having a single nucleotide polymorphism site by using a nucleic acid probe labeled with a fluorescent dye and measuring fluorescence of the fluorescent dye (see the method of "dynamic allele specific hybridization, DASH, on p. 16, 2nd paragraph and its more complete description in the article titled "Dynamic allele-specific hybridization" by Howell et al.) , and detecting the mutation on the basis of the result of the melting curve analysis, wherein the single nucleotide polymorphism is a mutation at the 3243rd position in a mitochondrial DNA (throughout the entire publication, especially the 2nd paragraph on p. 4 and claims 6, 28, 29 and 34).

Further regarding claim 18, Critchley teaches probes (see Abstract and see 1st full paragraph on p. 4) and teaches a sequence of 480 base comprising SEQ ID NOs: 21 and 22 (see sequence 13 on p. 9 of the sequence listings). There are 100% matches of SEQ ID NOs: 21 and 22 in this sequence as given in Table 1 below.

Table 1

100% Sequence Matches to SEQ ID NOs. 21 and 22

SEQ ID NO: 21	1	GGGCCCTGCCATCTTAAC	18	
Critchley's seq. 13	247	GGGCCCTGCCATCTTAAC	230	(reverse complement)
SEQ ID NO: 22	1	GGCCCTGCCATCTTAAC	17	
Critchley's seq. 13	246	GGCCCTGCCATCTTAAC	230	(reverse complement)

Regarding claim 19, Critchley teaches wherein a region containing the single nucleotide polymorphism site in a nucleic acid contained in a sample is amplified to obtain the nucleic acid showing the single nucleotide polymorphism (see the method of DASH on p. 16, 2nd paragraph and its more complete description in the article titled "Dynamic allele-specific hybridization" by Howell et al.

Regarding claim 20, Critchley teaches wherein the amplification is performed by a method using a DNA polymerase (see 1st full paragraph on p. 24 and as referenced there to the PCR methods of Froguet et al. (1993) *N Engl J Med* 328:697 who give PCR methods using a DNA polymerase, see title of reference no. 15 there).

Regarding claim 21, Critchley teaches wherein the amplification is performed in the presence of a nucleic acid probe (see the method of DASH, on p. 16, 2nd paragraph and its more complete description in the article titled "Dynamic allele-specific hybridization" by Howell et al.).

Claim 18 is rejected for SEQ ID NOs: 21 and 22, as described following.

With regard to Claim 18, Critchley disclose probes to sequence 13. Critchley does not specifically teach sequences consisting of SEQ ID NO: 21 or SEQ ID NO: 22. It is noted that the instant probe sites of SEQ ID NOs: 21 and 22 are contained within the sequence disclosed by Critchley, as given in Table 1 above.

The above described references do not specifically disclose the identical probe sequences of SEQ ID NOs: 21 and 22 used in the claimed invention.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious.

Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed probes simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for probes of the mutation

Art Unit: 1637

at the 3243rd position in a mitochondrial DNA and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck et al (1999) expressly provides evidence of the equivalence of primers/probes. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer/probe would have a reasonable expectation of success.

Art Unit: 1637

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Critchley by using any number of probes to the sequence disclosed by Critchley as suggested by Buck et al. with a reasonable expectation of success. The motivation to do so is provided by Buck et al. who teach that a multitude of primers/probes to a given sequence give excellent results (entire article, especially the *Discussion* section). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

6. No claim is free of the prior art.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

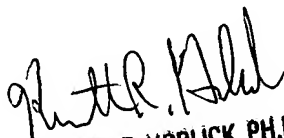
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner
Art Unit 1637
October 22, 2007

MS


KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
10/22/07